THE EVOLUTION OF NEW IMAGING TECHNOLOGIES

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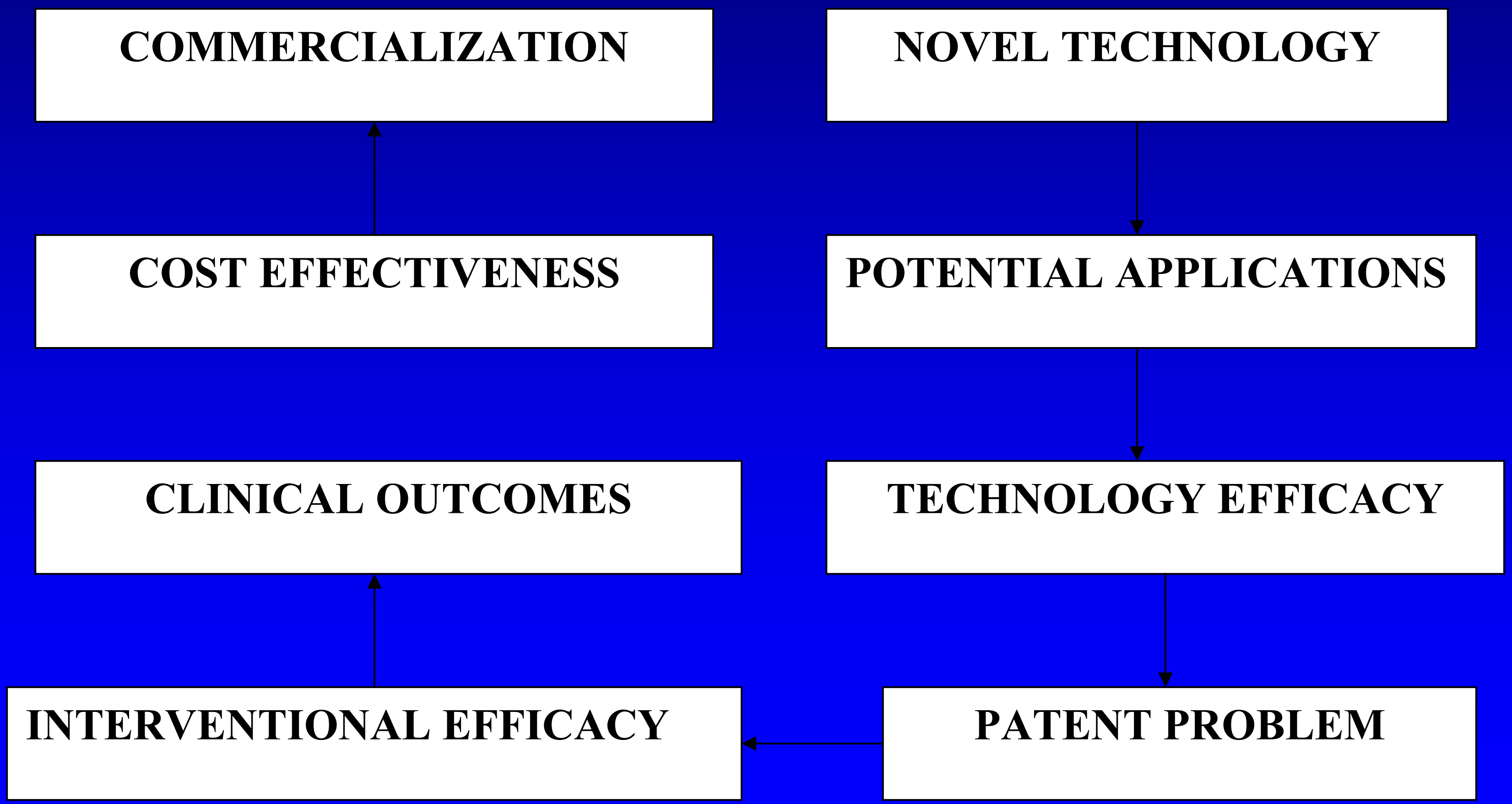
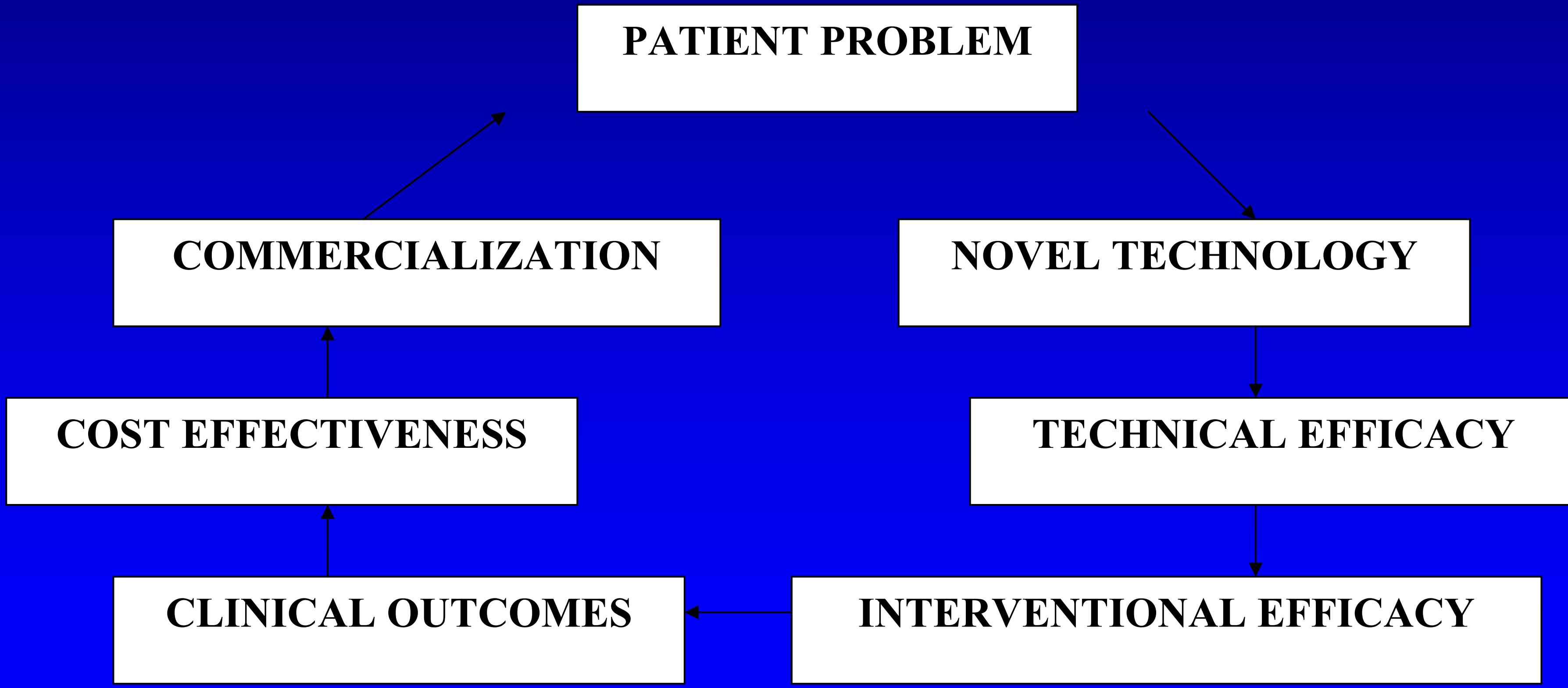
MODELS OF TECHNOLOGY EVOLUTION

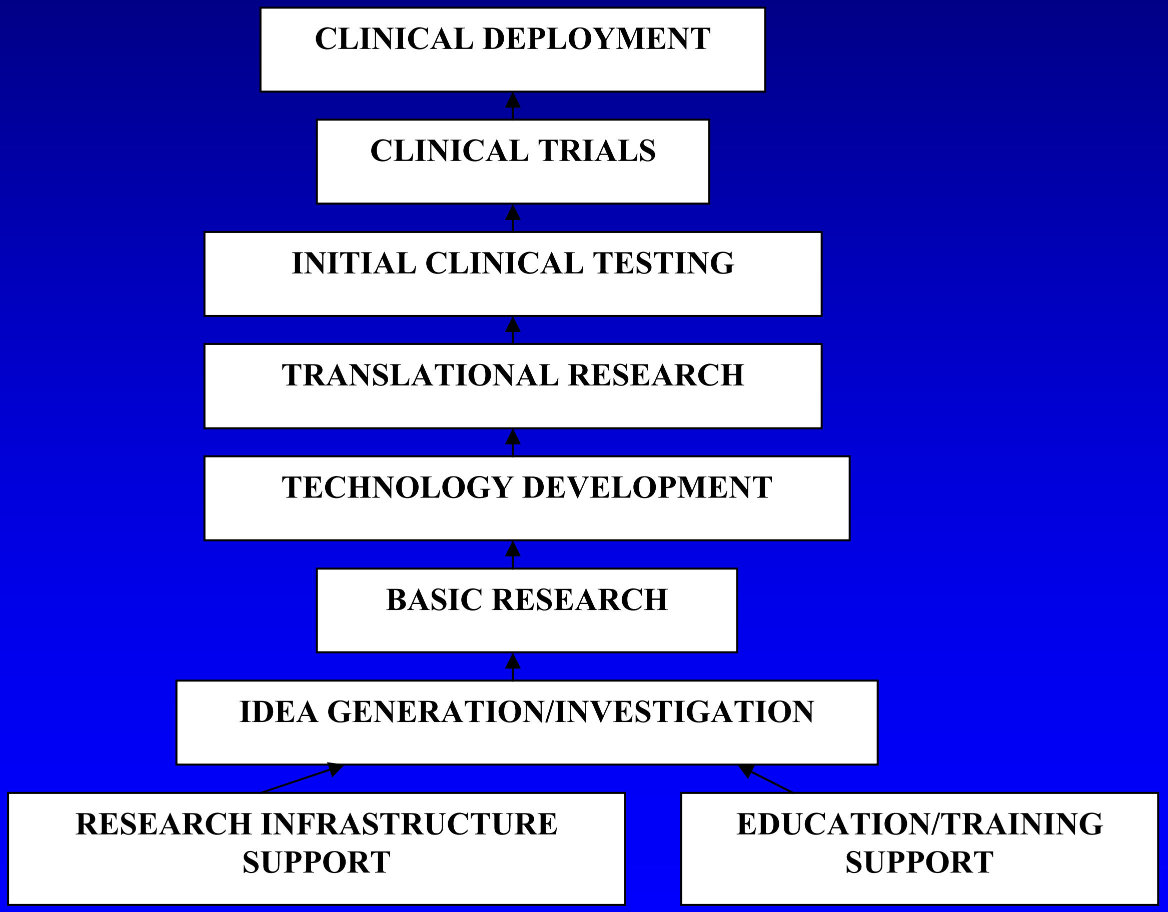
TECHNOLOGY EVOLUTION THROUGH TECHNOLOGY PUSH



TECHNOLOGY EVOLUTION THROUGH CLINICAL PULL



SYSTEMS APPROACH TO TECHNOLOGY DEVELOPMENT



SYSTEMS MODEL FOR TECHNOLOGY DEVELOPMENT

- Team approach
- Effective communication
- Endorsement by institution
- Investment in high risk, high impact ideas
- Technology-driven and hypothesis-driven research support

SYSTEMS MODEL FOR TECHNOLOGY DEVELOPMENT (cont'd)

- Evolutionary (incremental) and revolutionary (quantum leap)
- Consensus-building approach
- Realistic cost and time estimates
- Development chilled by excessive regulation

SYSTEMS MODEL FOR TECHNOLOGY DEVELOPMENT (cont’d)

- Evaluation steps: validation, efficacy, efficiency
- Both engineering and clinical validation
- Evaluation: faster, better, cheaper
- Intermediate and final endpoints

PRECLINICAL STUDIES

- Animal models with specific diseases
- Models and intervention endpoints scaled to humans
- Consensus criteria for intervention evaluation

SPATIAL SCALING OF IMAGING

- Man → Mouse: 15x dimensional ↓, 3400x volume ↓
- As volume ↓, signal/noise ↓
- Challenge of developing animal imaging devices
- Need for intervention by Federal sources

IDENTIFICATION OF INTERVENTIONAL TARGET

- Spatial/temporal image fusion
- Combine anatomic and functional information
- Real-time data acquisition/display/analysis
- In vivo pathological analysis
- Identify target boundaries
- Biologically-correct interventions

IMAGE CHALLENGES/OPPORTUNITIES

- Image atlases, data libraries, algorithm/software sharing
- Agreed-upon image/data transfer protocols
- Software/hardware limitations recognized/accommodated
- Images matched to clinical requirements
- 3D/4D images
- Imaging may include depiction/intervention/evaluation
- New catheter materials/interventional techniques

EDUCATION/TRAINING FOR TECHNOLOGY DEVELOPMENT

- Mentor oversight
- Multi-modality information in real time
- Collaborative education/training
- Exploratory culture
- Engineering/Imaging Integration
- Dedication to research

Physiologic MR Imaging of Brain Tumors

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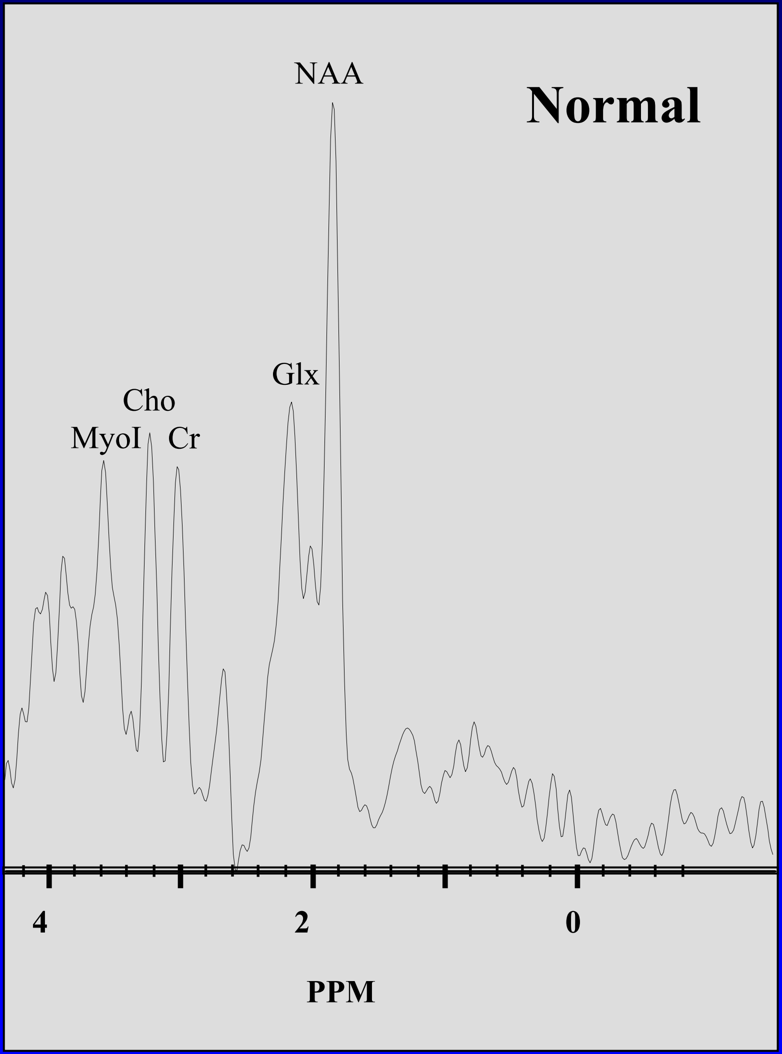
Physiologic Brain Imaging

- Standard MRI: Image based assessment of brain morphology
- Physiologic MRI: Image based assessment of brain physiology and pathophysiology
  - MR Spectroscopy - brain metabolites
  - MR Perfusion - cerebrovascular physiology
  - FMRI - cortical/subcortical activation
  - Diffusion/DTI - molecular motion
  - MT/Spin-lock - macromolecular environments
  - Oxygen extraction - energy metabolism
  - Molecular imaging – chemical metabolism
  - Others

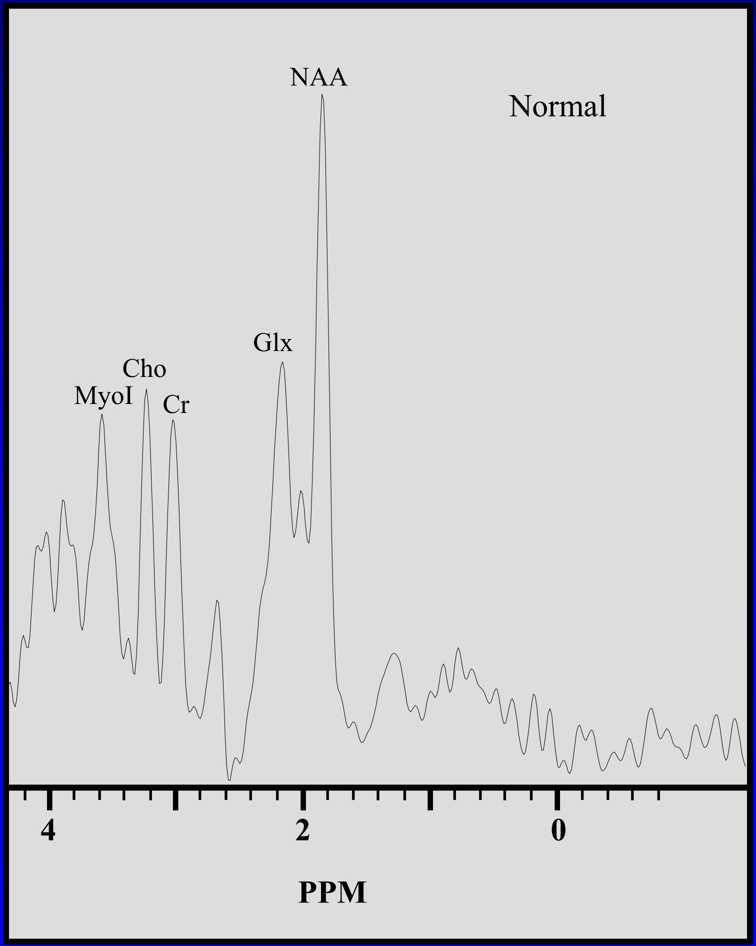
Proton MRS

- Normal metabolites
  - Myo-inositol (MyoI) = 3.6 ppm, 5 mM
  - Choline (Cho) = 3.25 ppm, 1.5 mM
  - Creatine/phosphocreatine (Cr) = 3.0 ppm, 8 mM
  - Glutamate/glutamine (Glx) = 2.2-2.4 ppm, 5 mM/10 mM
  - N-acetylaspartate (NAA) = 2.0 ppm, 10-15 mM
- Common abnormal metabolites
  - Lactic acid (Lac) = 1.33 ppm (at 1.5T)
  - Mobile lipids (Lip) = 0.9 and 1.3 ppm

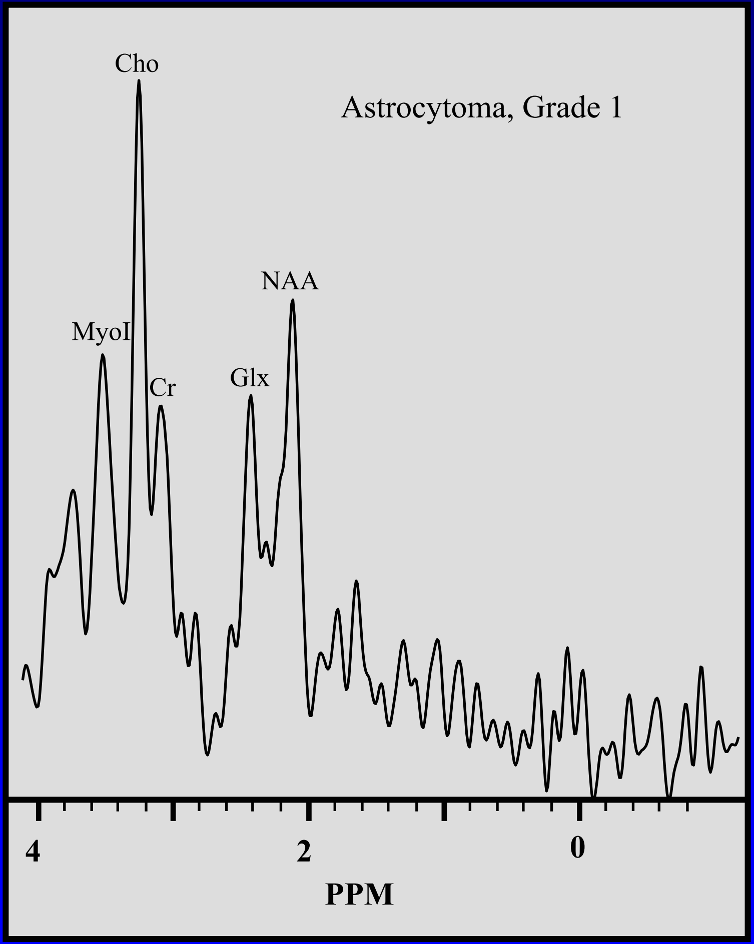


Proton MRS : Tumor Profile

Normal



Tumor

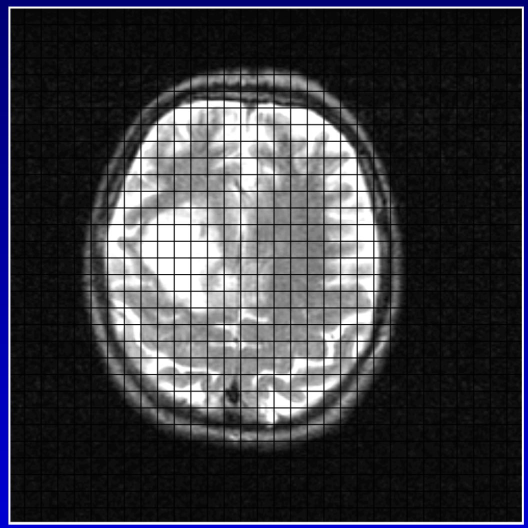


Potential Clinical Applications of Proton MRS in Tumor Patients

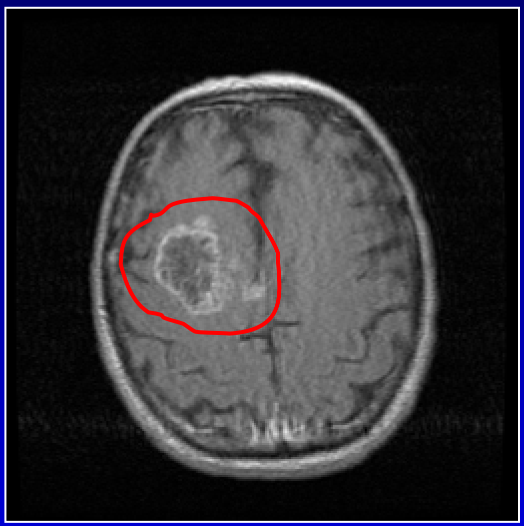
- Differentiate tumor from non-tumor
  - Cho/NAA = 85% accuracy alone
  - 95% accuracy considering all peaks
  - >95% accuracy by adding morphologic criteria
- Determine zones of highest mitotic activity
  - Biopsy
  - Resection
- Detect occult disease
  - Treatment planning
- Recurrent disease
  - Differentiate recurrence from XRT necrosis

55 Year Old Male with a GBM, Undergoing Radiation Treatment planning

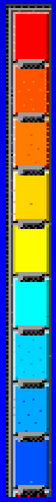
Standard (T2) Image



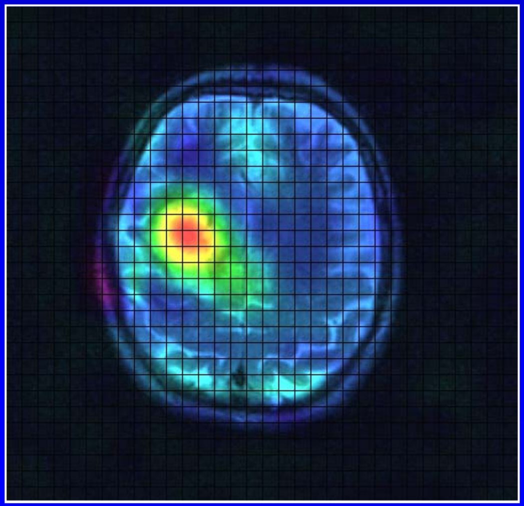
Radiation Target Area



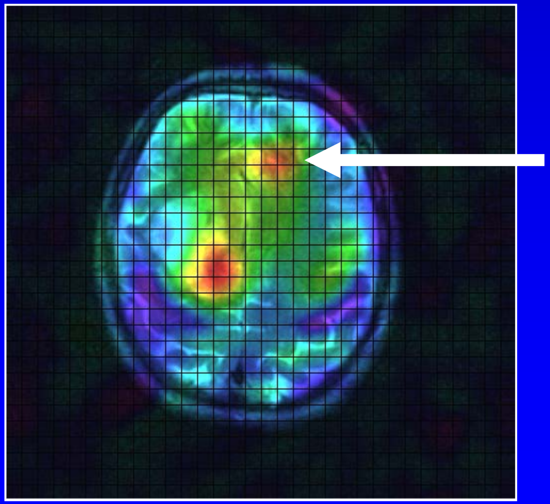
High



Low



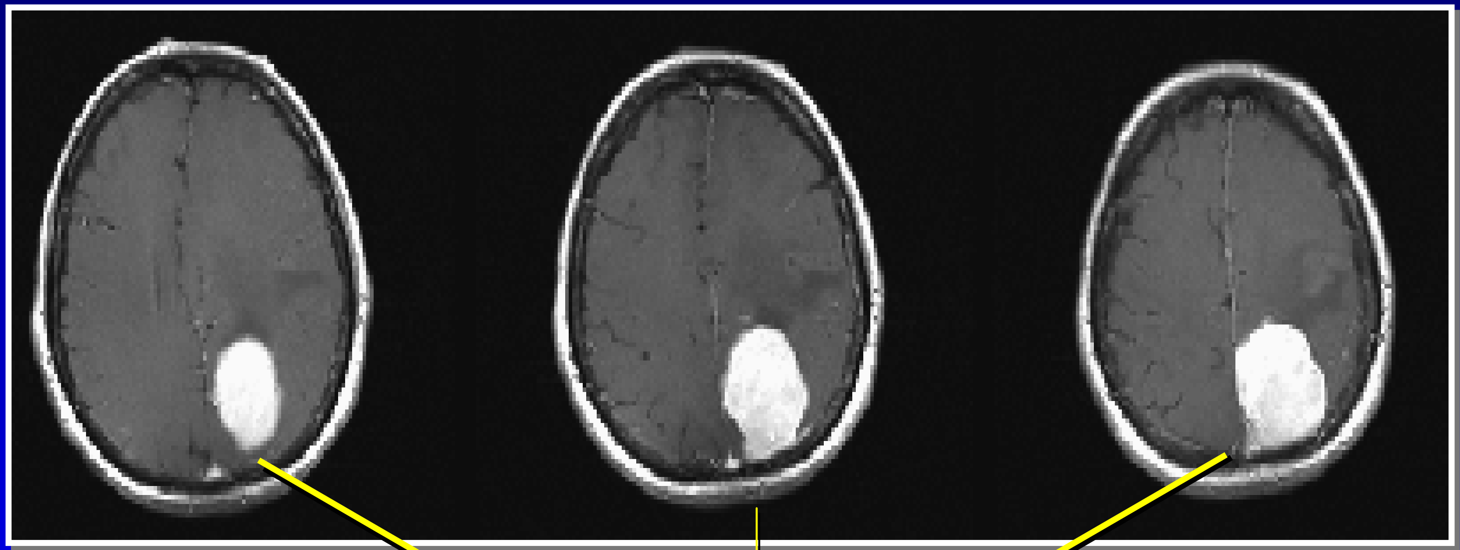
Lactic Acid + Lipid Image



Choline Image

Unexpected focus of mitotic activity (tumor) in <u>opposite</u> hemisphere

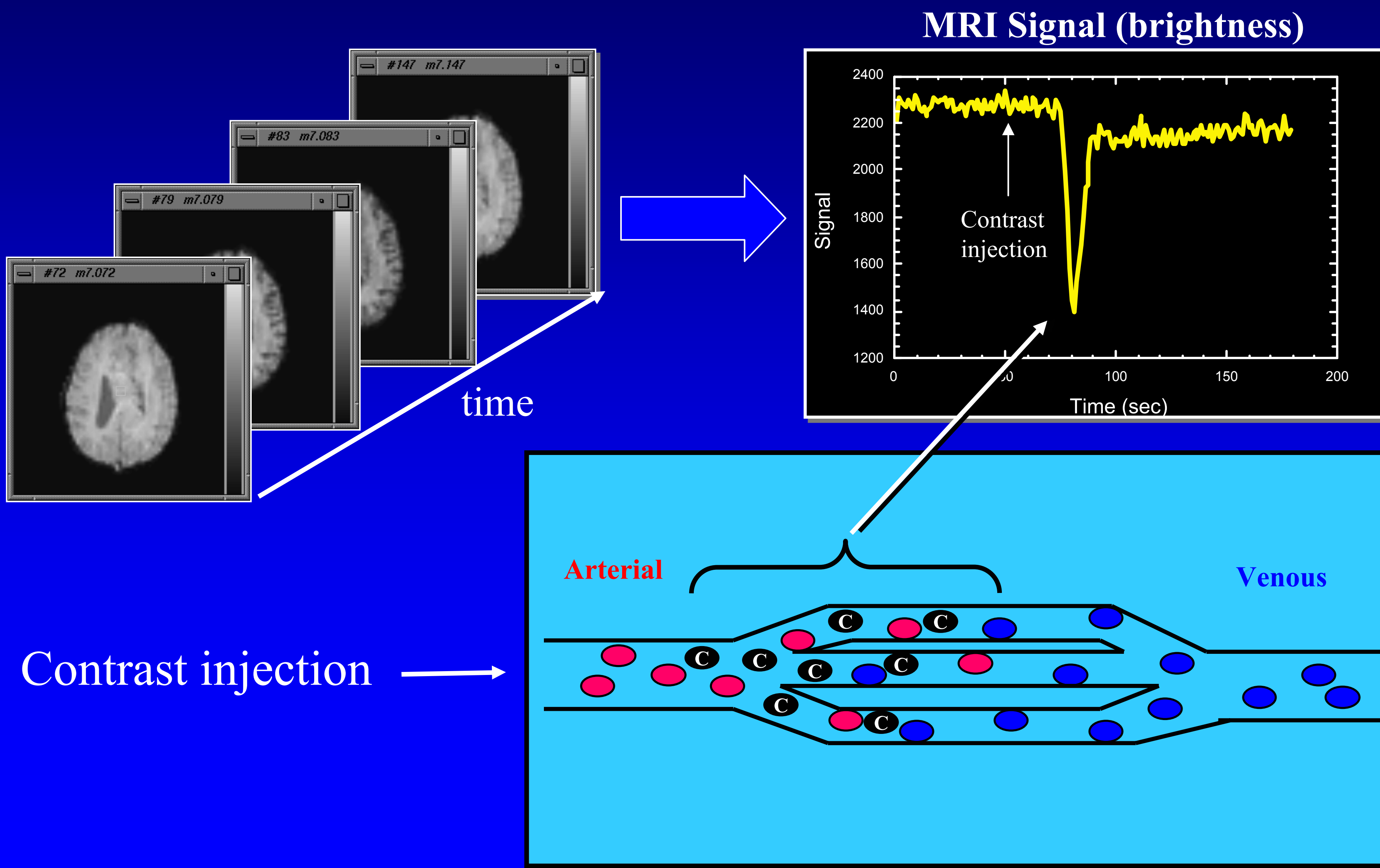
Standard Practice: Contrast Agent MRI

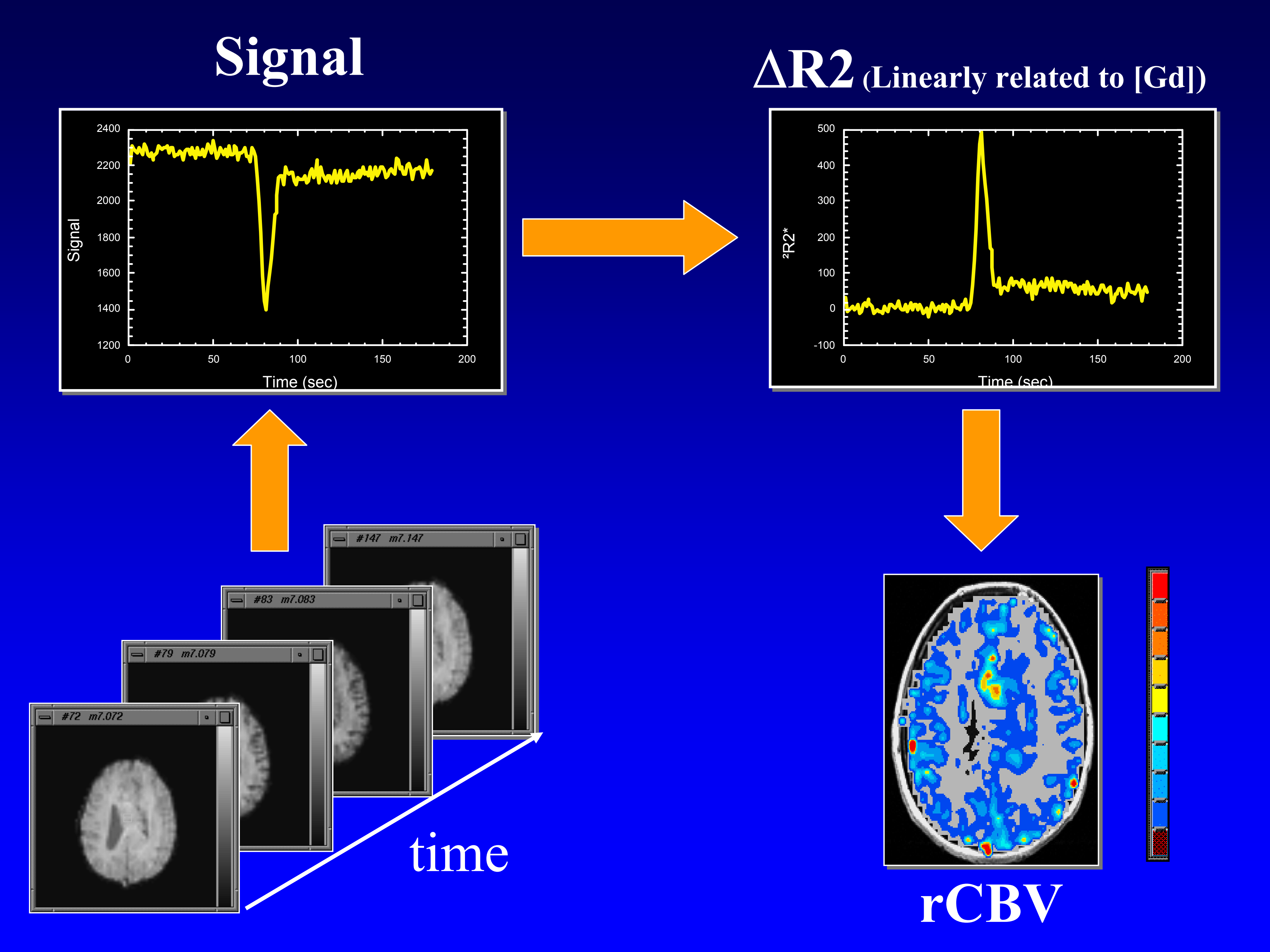


Uptake of contrast agent in tumor

Not specific for tumor vascularity !!

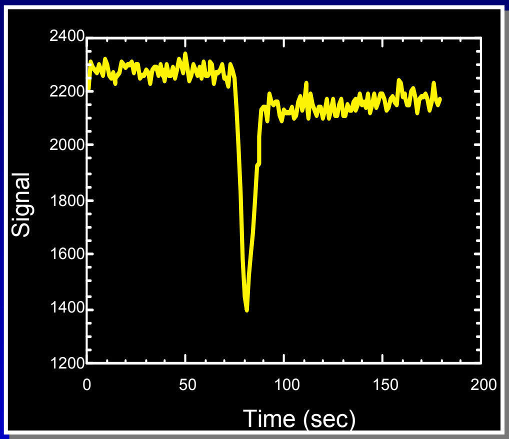
Cerebral Vascular Imaging



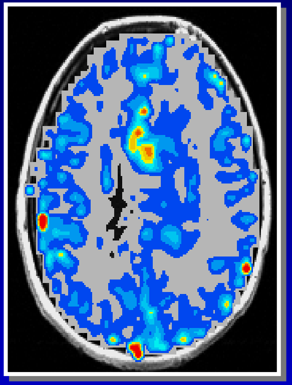

Signal
ΔR2 (Linearly related to [Gd])
Signal
2400
2200
2000
1800
1600
1400
1200
0
50
100
150
200
Time (sec)
²R2*
500
400
300
200
100
0
-100
0
50
100
150
200
Time (sec)
#147 m7.147
#83 m7.083
#79 m7.079
#72 m7.072
time
rCBV

Collect GE & SE Data:

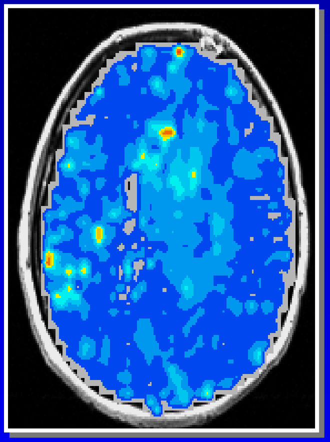
GE Signal

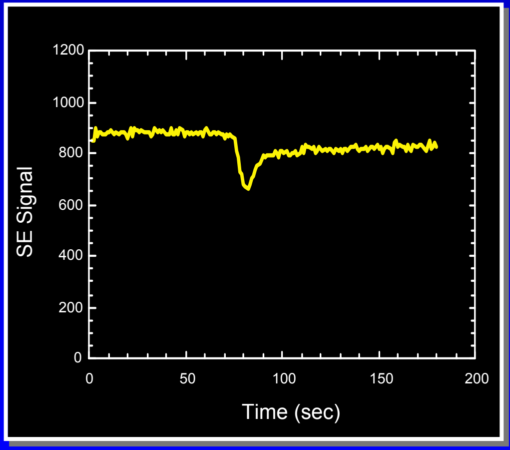


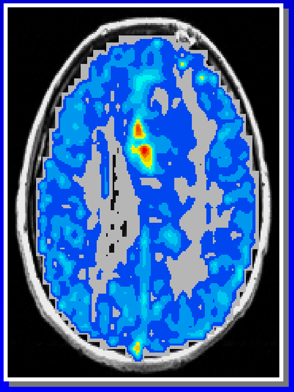
TOTAL rCBV



Vessel diameter



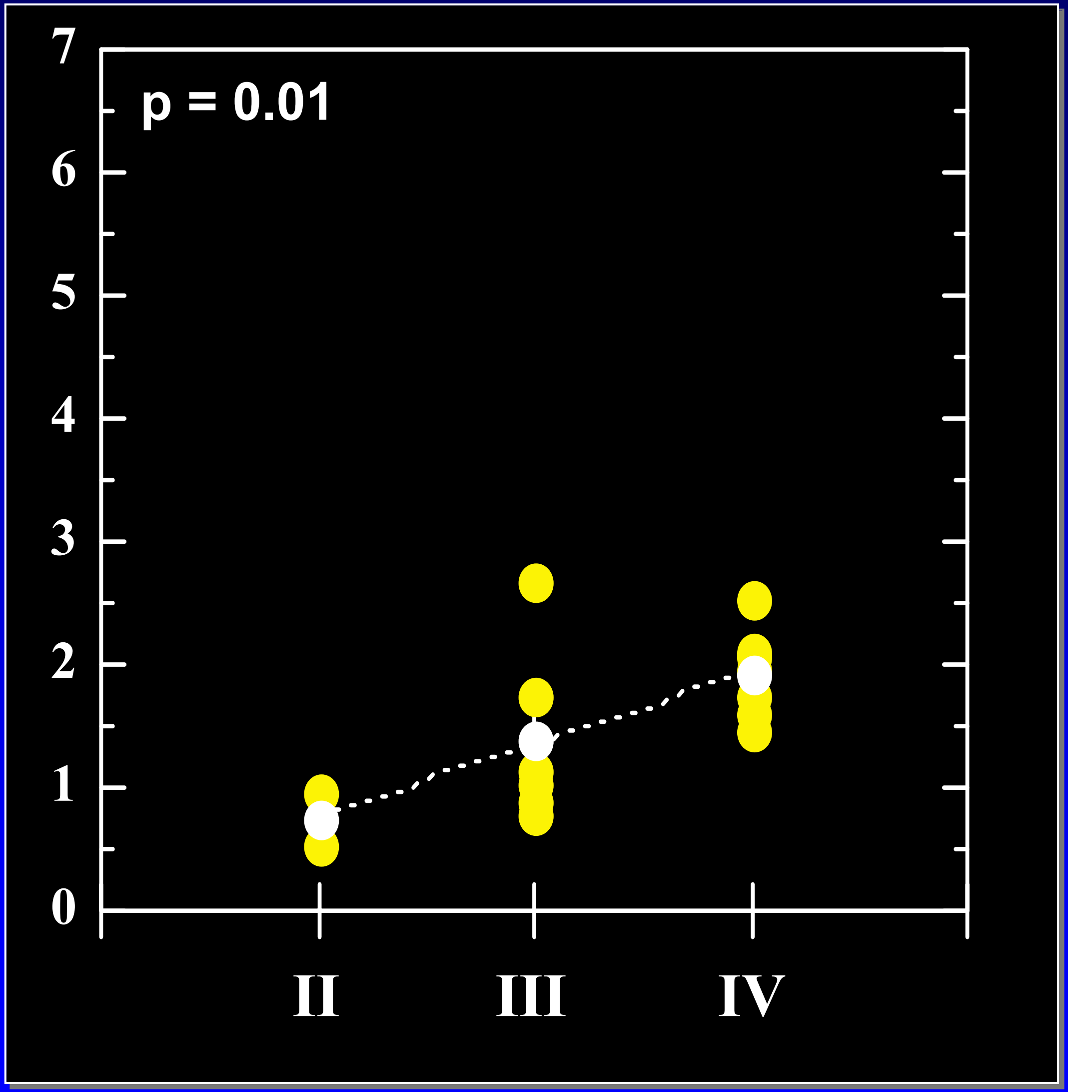




SE Signal

Microvascular rCBV
(7-10 microns)

Vessel Diameter

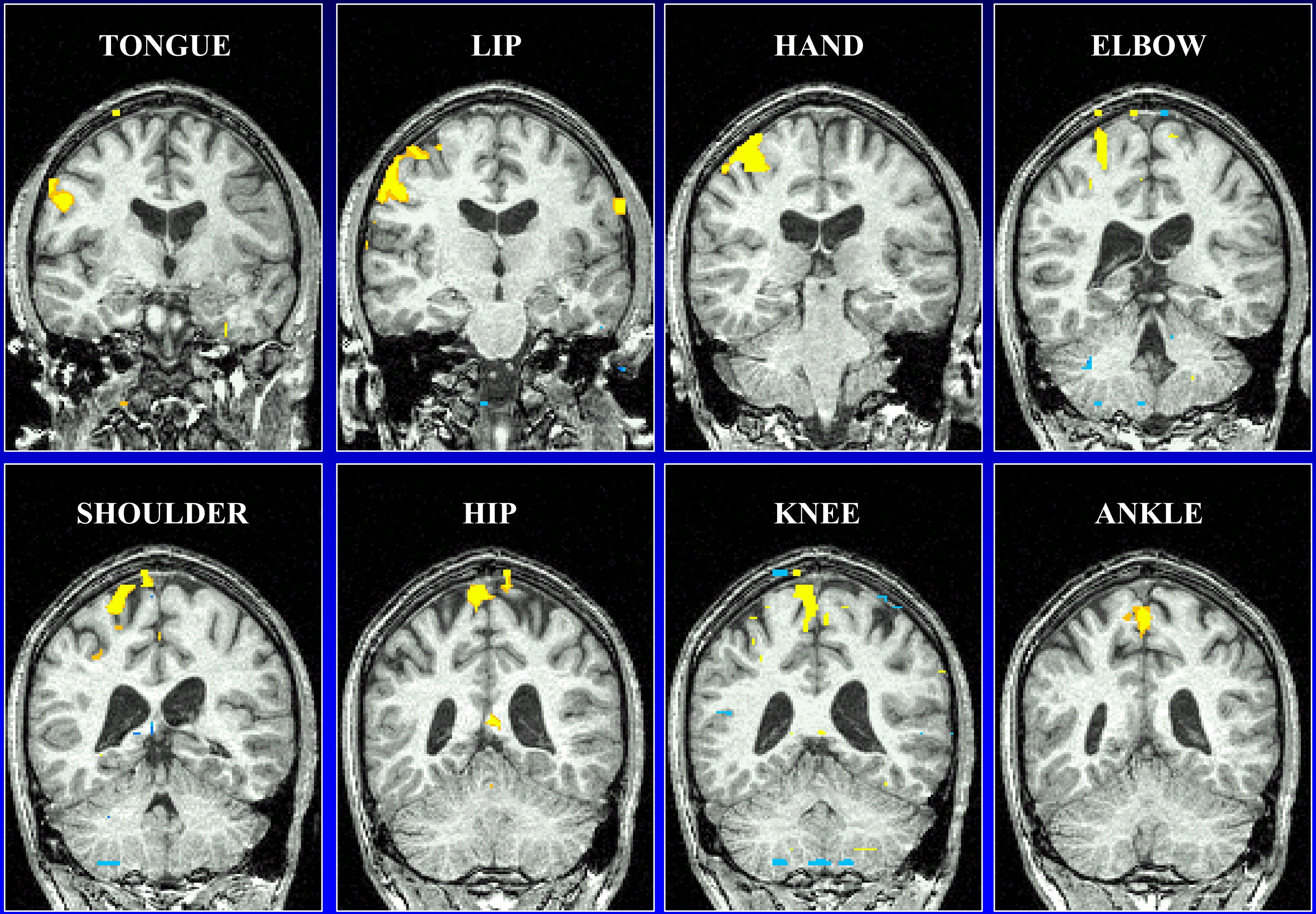


Potential Applications of rCBV Imaging in Tumor Patients

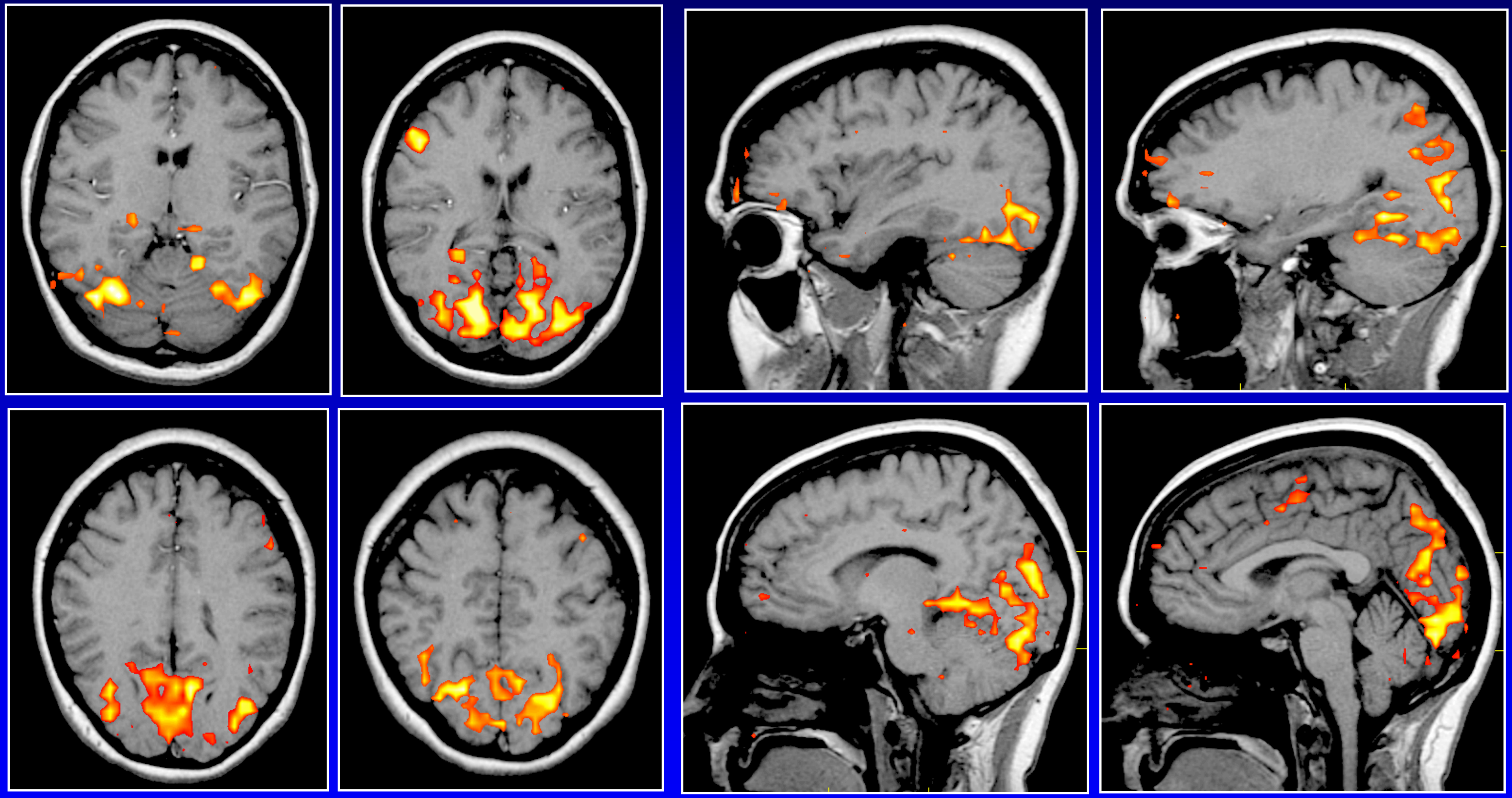
- Suggest tumor grade
  - 75% accuracy
- Pre-operative planning
  - Optimize biopsy
  - Reduce complications
- Recurrent tumor
  - Differentiate recurrent tumor from gliotic tissue
  - Differentiate recurrent tumor from XRT necrosis
- Detection of grade conversion

Functional Magnetic Resonance Imaging (FMRI)

Mapping the Sensori-motor Homunculus



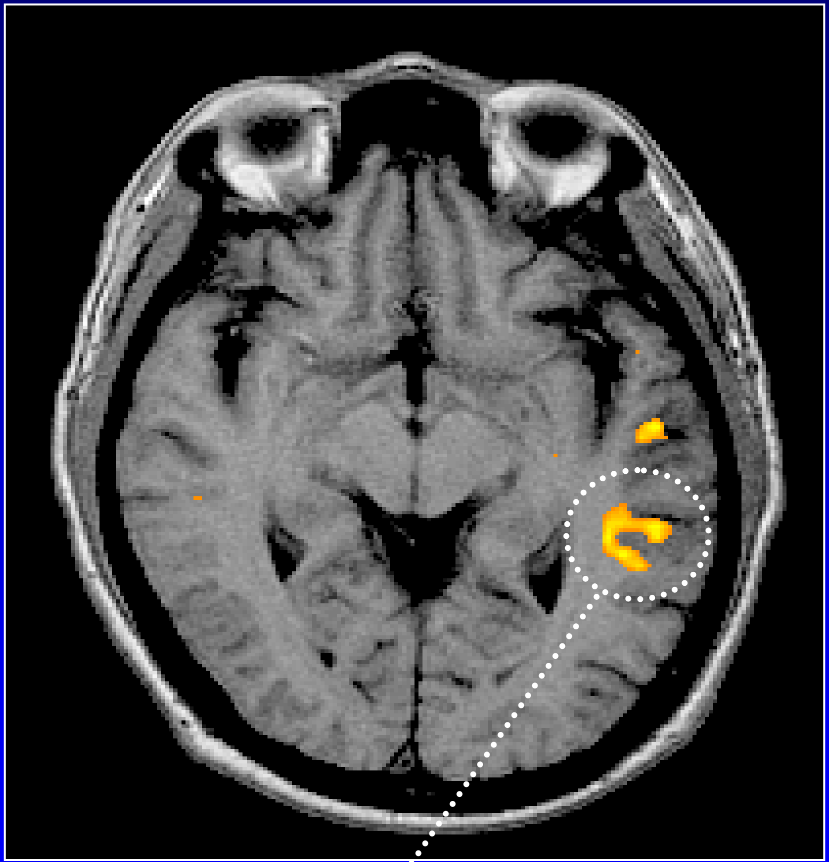
Mapping Visual Function



Rotating Checker Board

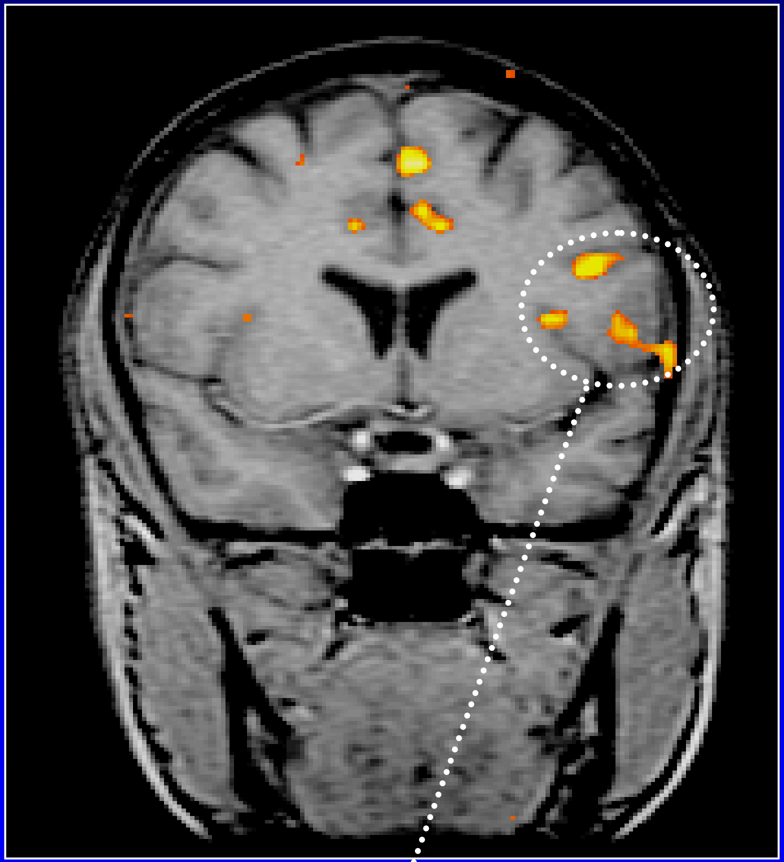
Mapping Language Function

Subtraction Auditory Language Task



Posterior language area
(Planum temporale)

Covert Word Generation Task

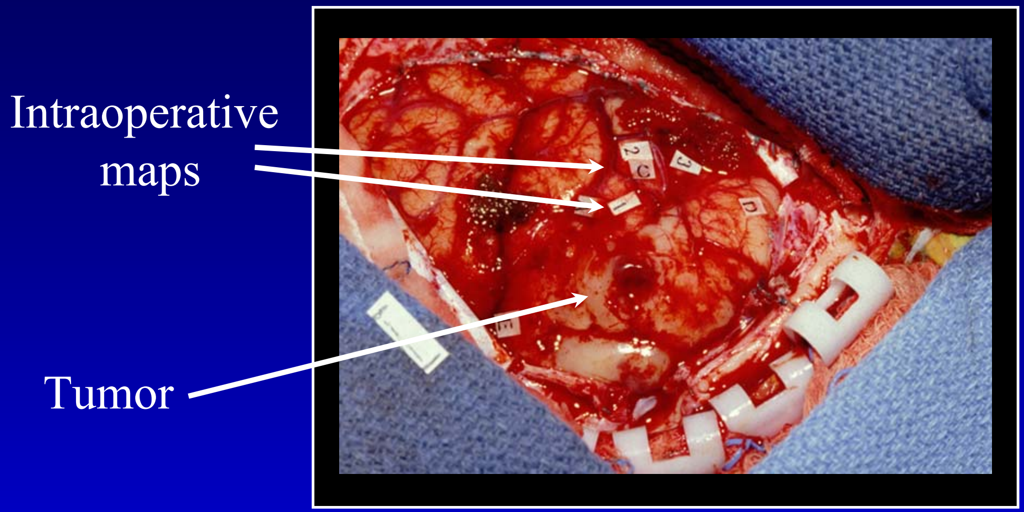


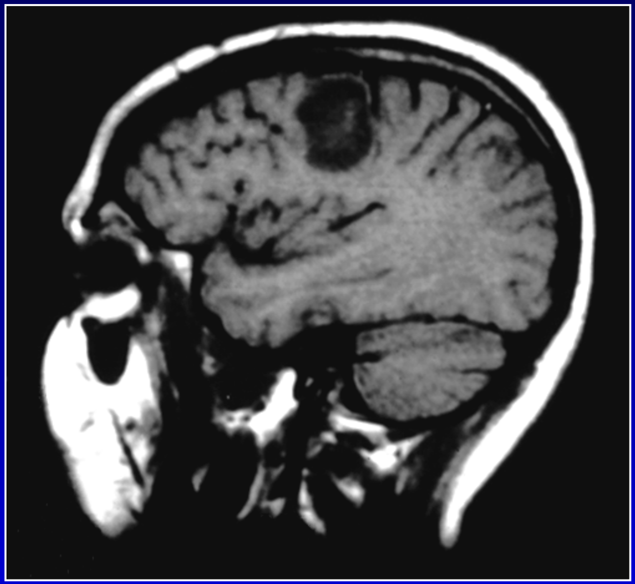
Frontal language area
(IFG)

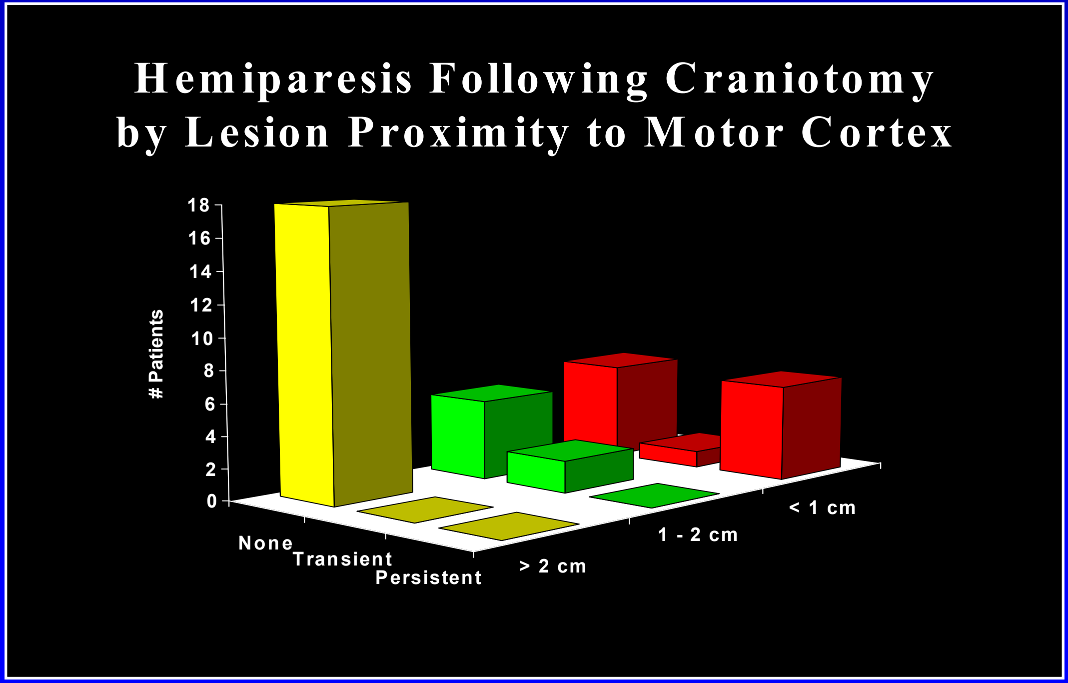
Potential Clinical Applications of BOLD FMRI in Tumor Patients

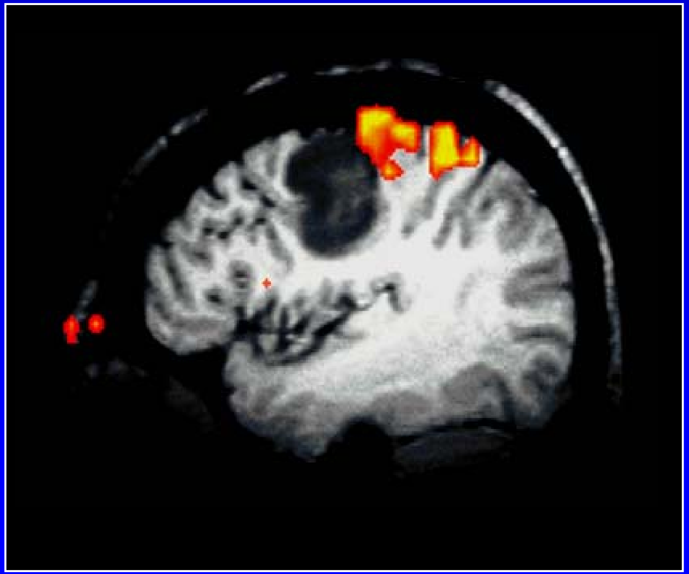
- Mapping eloquent cortex
  - Pre-operative planning
  - Risk assessment
- Enhancing white matter tractography
  - Identify specific white matter tracts
- Tumor energy metabolism

FMRI OF ELOQUENT MOTOR CORTEX:
Correlation with postoperative deficit

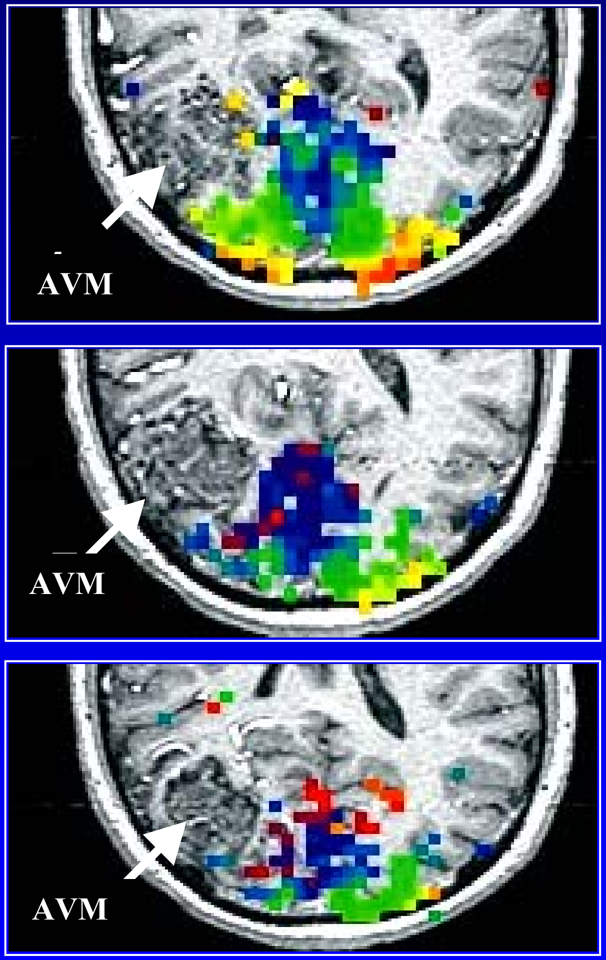




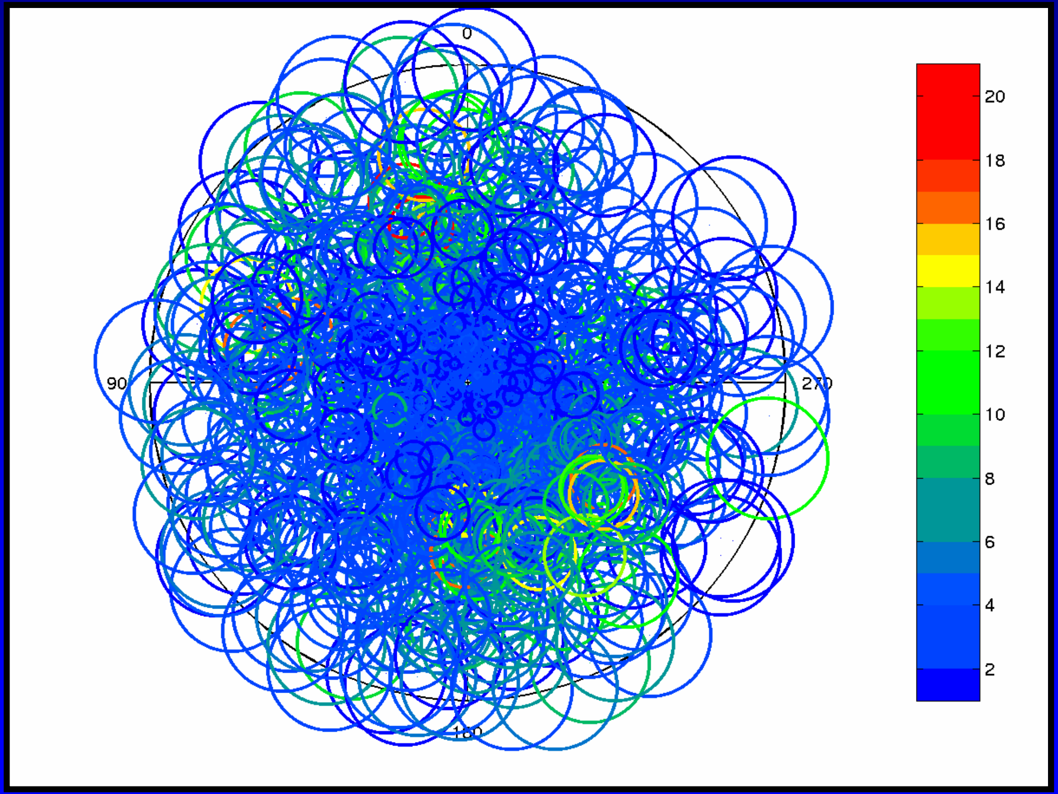




41 yo with an occipital AVM



Functional Field Map



Case Illustration

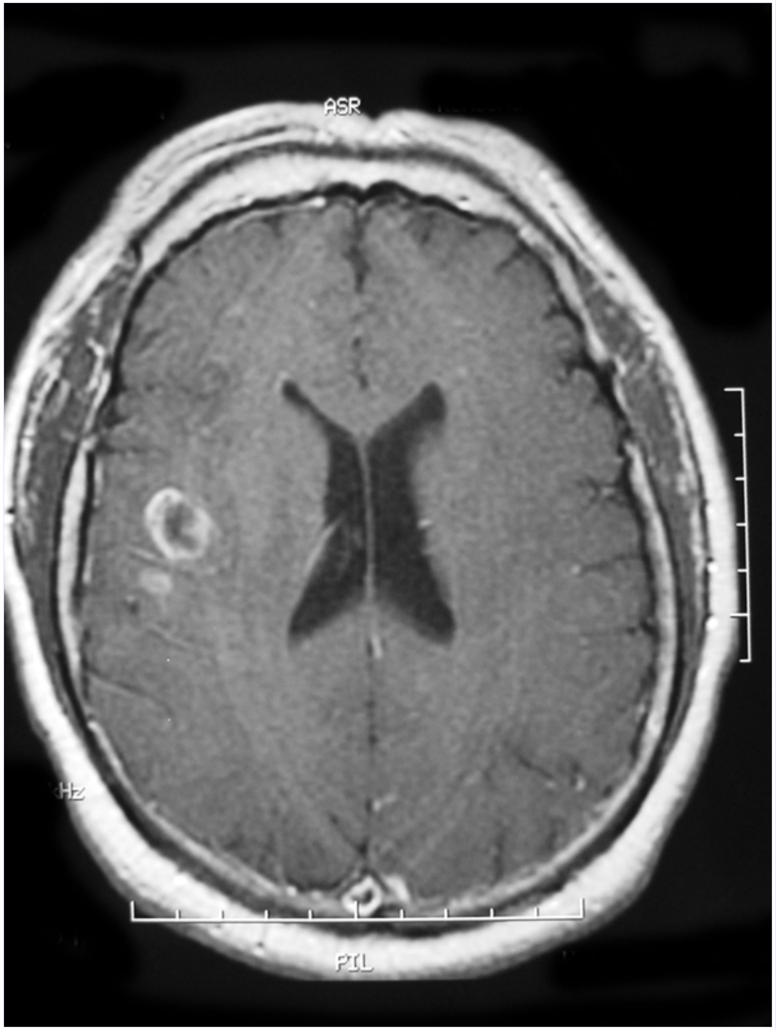
- 41 year old Hispanic male with left upper extremity (hand) paresthesias

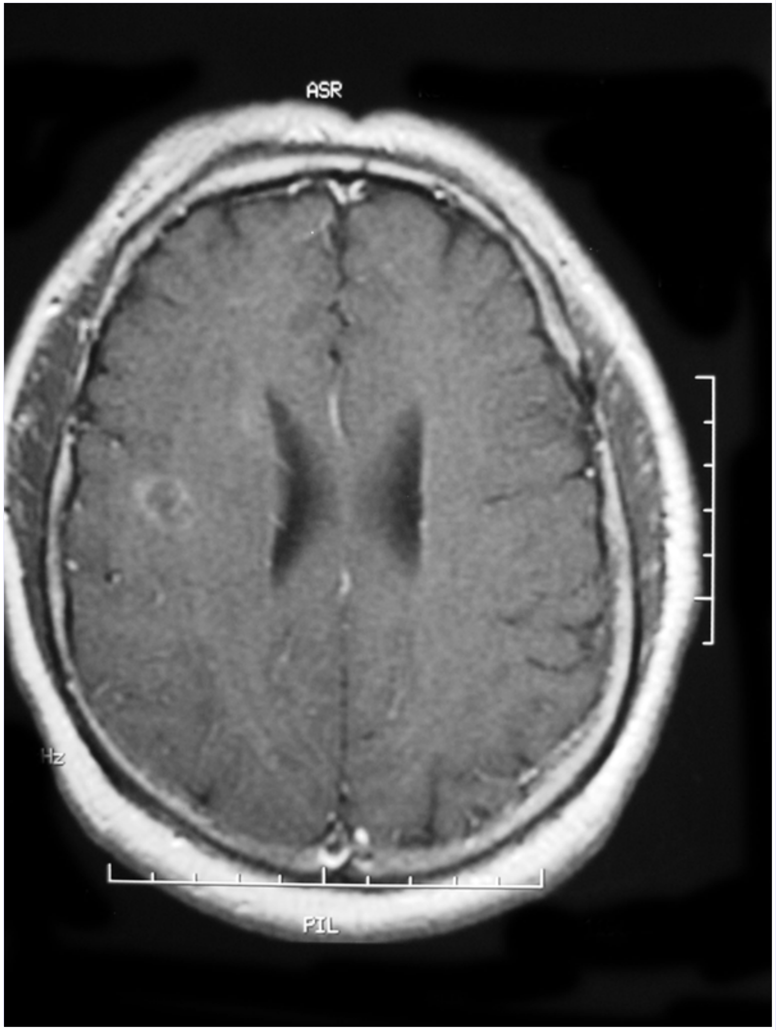
41yo with LUE paresthesias - CT

41yo with LUE paresthesias

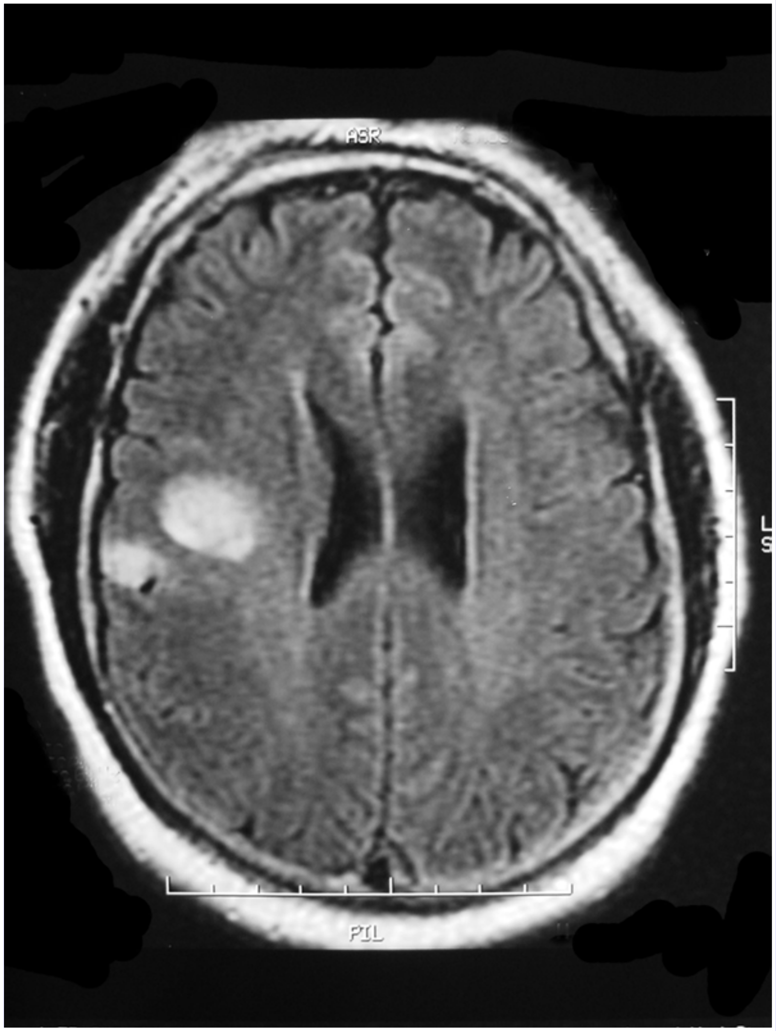
- Small right hemisphere lesion
  - Primary brain tumor
  - Bacterial abscess
  - Parasitic abscess
  - Tuberculous abscess
  - Fungal abscess
  - Stroke
  - MS
  - Vascularity?
  - Relationship to eloquent cortex?

41yo with LUE paresthesias - T1 Gd

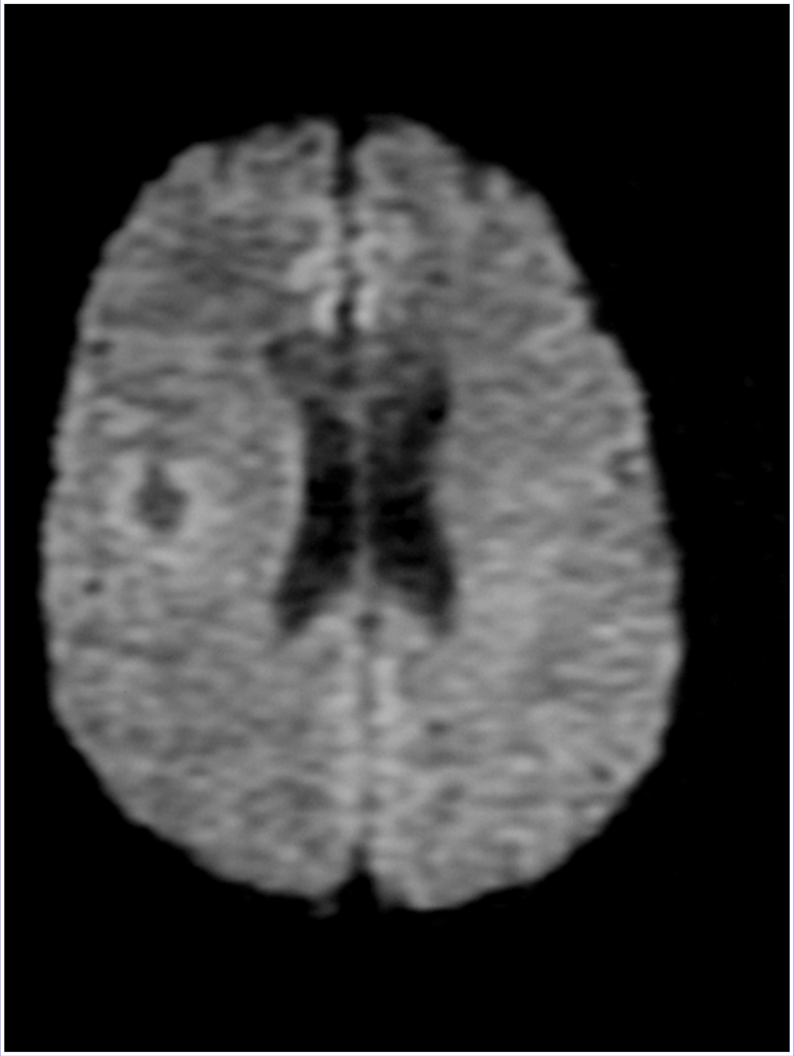




41yo with LUE paresthesias - FLAIR



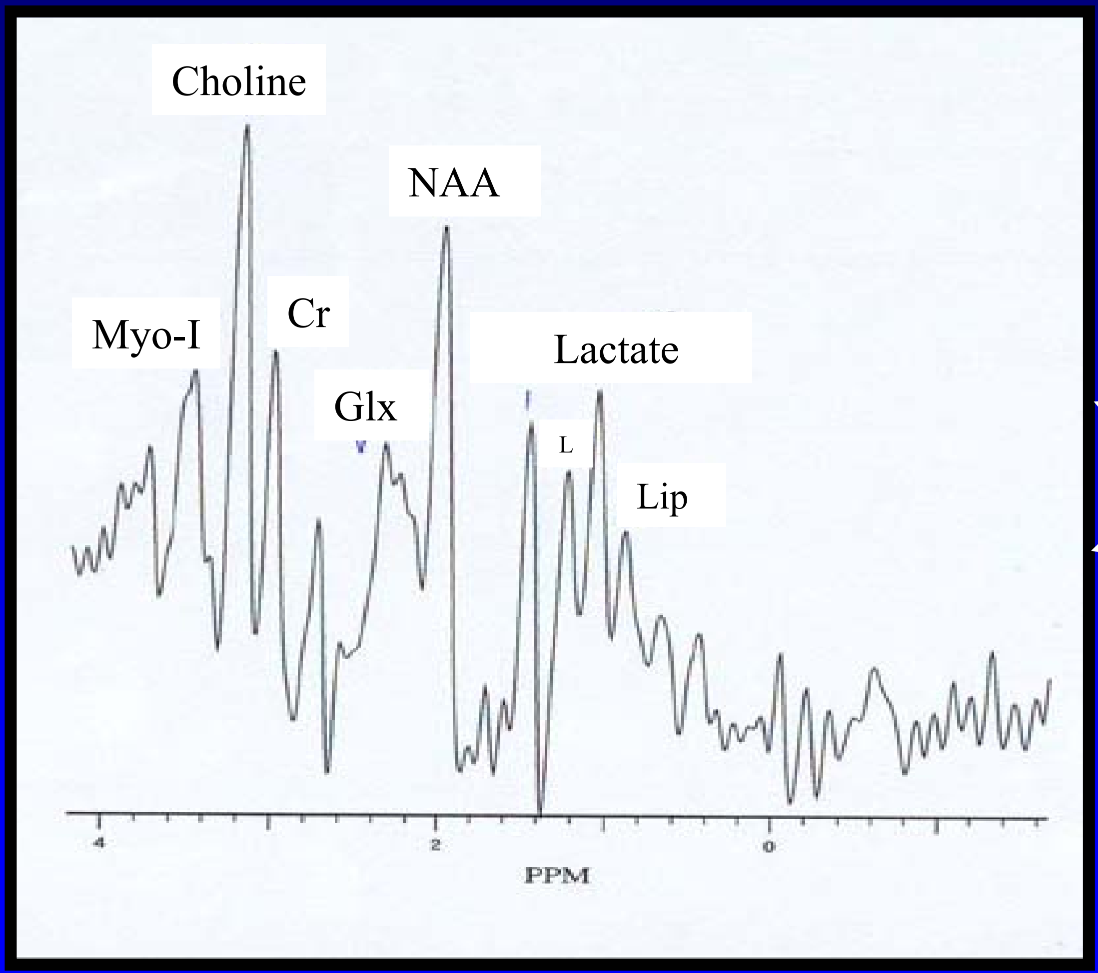
41yo with LUE paresthesias - DWI



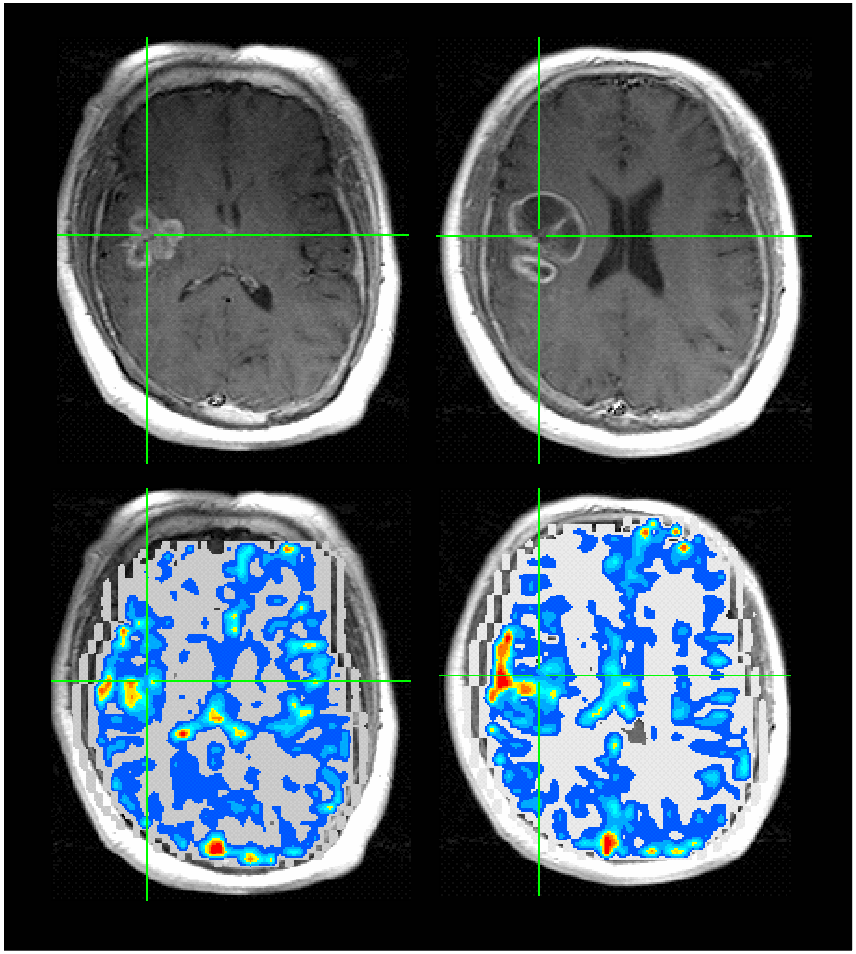
41yo with LUE paresthesias

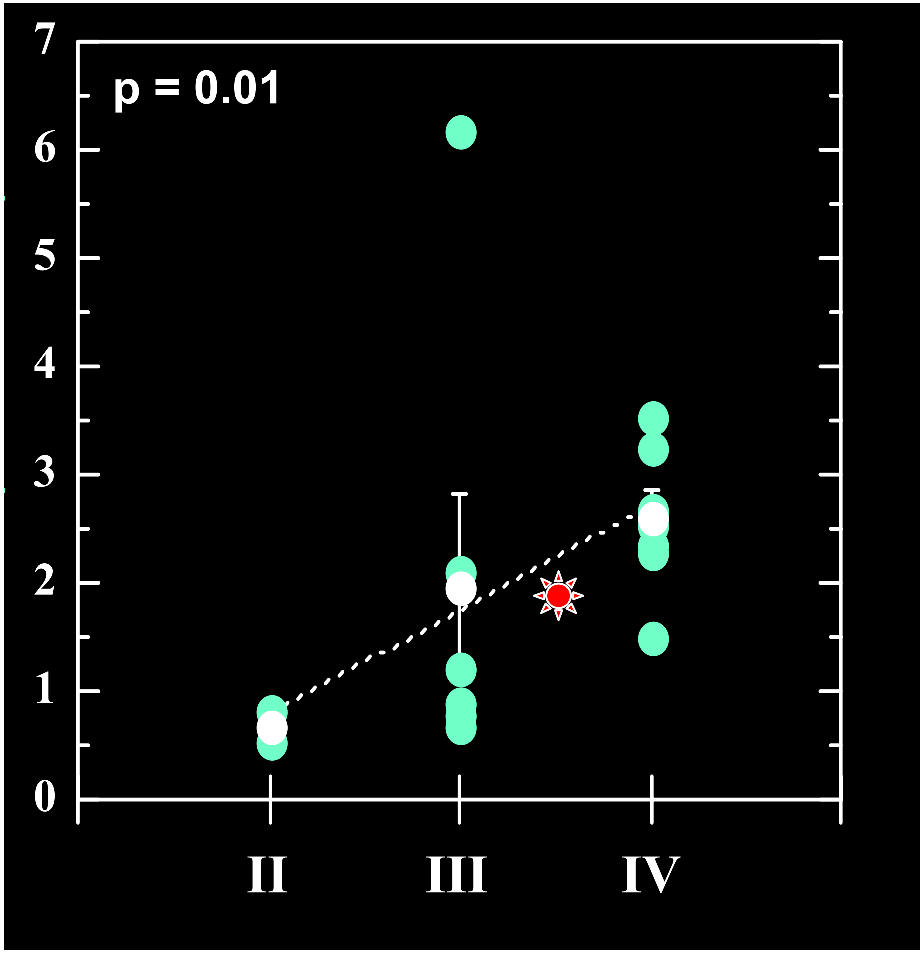
- Small right hemisphere lesion
  - Primary brain tumor
  - Bacterial abscess
  - Parasitic abscess
  - Tuberculous abscess
  - Fungal abscess
  - Stroke
  - MS
  - Vascularity?
  - Relationship to eloquent cortex?

41yo with LUE paresthesias- MRS



41yo with LUE paresthesias - corrected rCBV (✹)

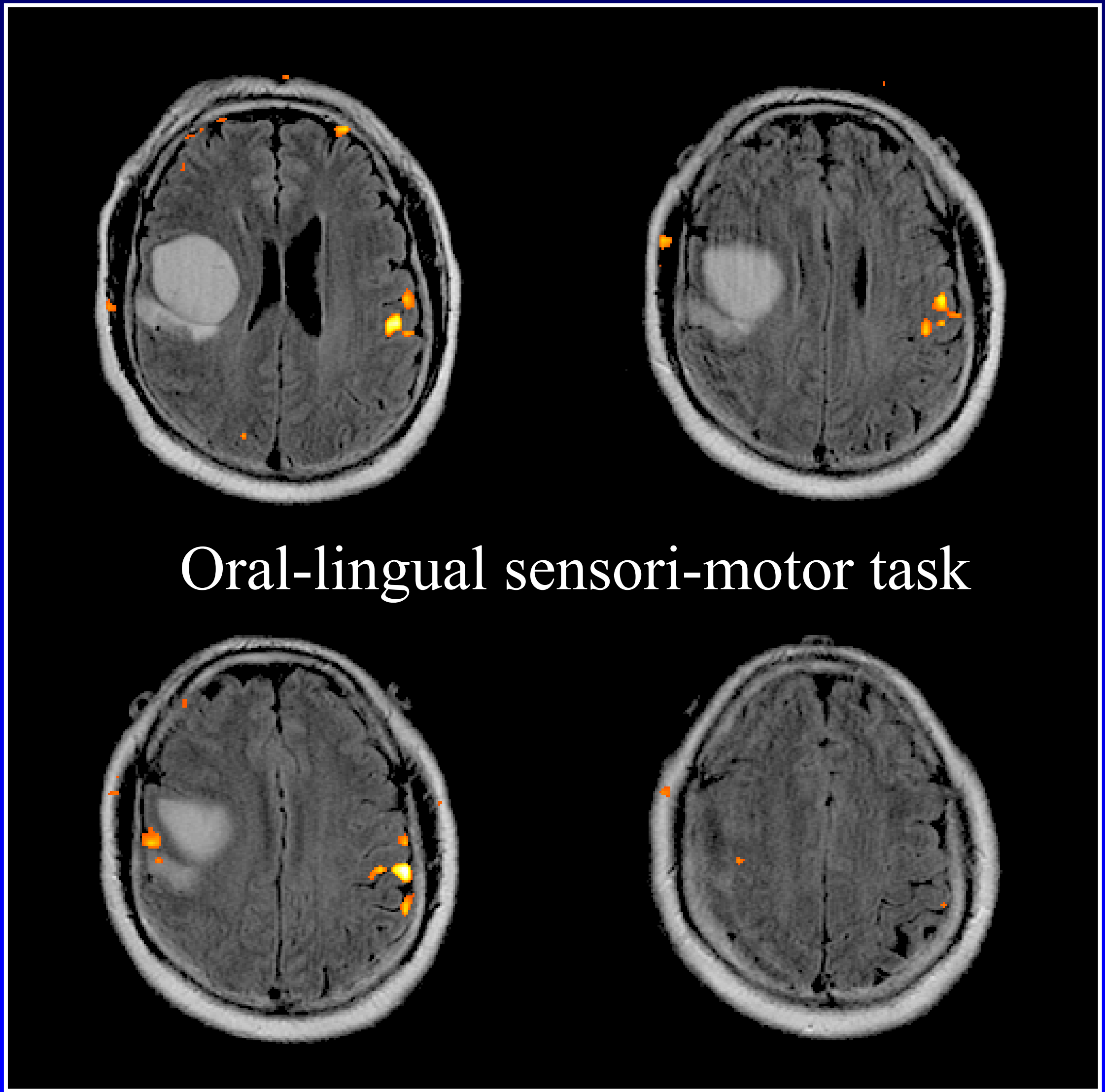




41yo with LUE paresthesias

- Small right hemisphere lesion
  - Primary brain tumor (GBM)
  - Bacterial abscess
  - Parasitic abscess
  - Tuberculous abscess
  - Fungal abscess
  - Stroke
  - MS
  - Vascularity increased inferio-laterally and consistent with grade IV glioma
  - Relationship to eloquent cortex?

41yo with LUE paresthesias - FMRI



41yo with LUE paresthesias

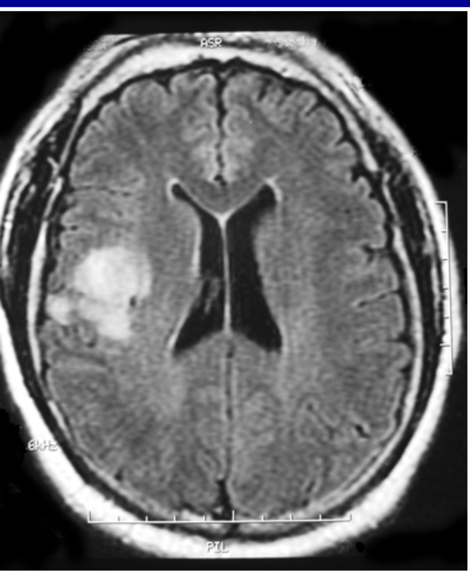
- Small right hemisphere lesion
  - Primary brain tumor (GBM)
  - Bacterial abscess
  - Parasitic abscess
  - Tuberculous abscess
  - Fungal abscess
  - Stroke
  - MS
  - Vascularity increased inferio-laterally and consistent with grade IV glioma
  - Involvement of oral-lingual cortex

Tumor Activity and Growth

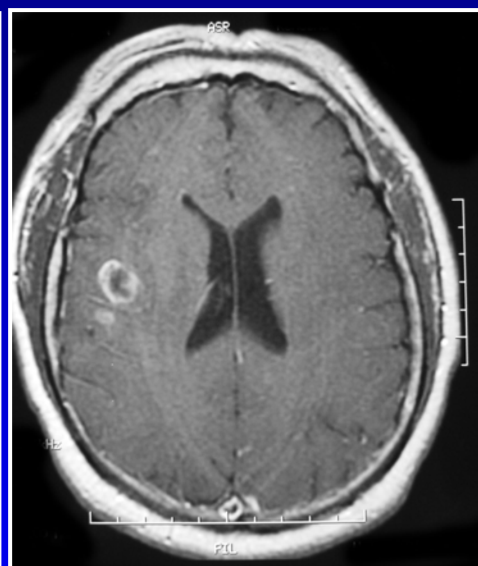
Conventional Imaging

2DCSI

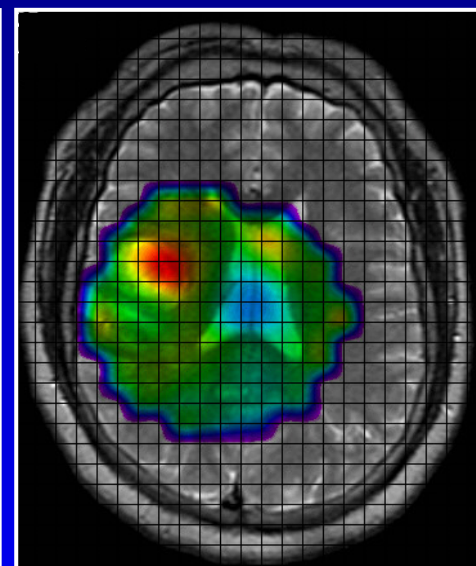
Tumor Growth



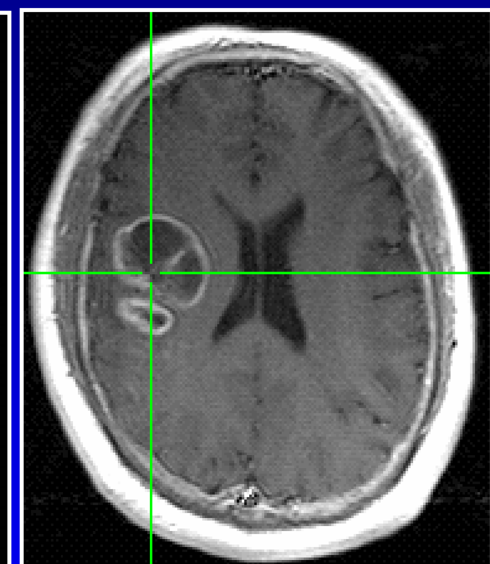
Flair



T1-Gd



Cho/NAA



T1-Gd several weeks later

Presentation

41yo with right hemisphere lesion

- Right hemispheric glioblastoma multiforme with neovascularity at the inferio-lateral edge
- Highest tumor growth/activity at the medial border, in proximity to the sensori-motor white matter tracts
- Tumor is removed from the left LUE and LLE primary motor cortex, but involves the oral-lingual sensori-motor cortex risking a facial hemiparesis with surgery
- Seizure activity is suggested in proximity to the primary LUE sensory cortex, corresponding to a clinical picture of sensory seizures, without direct LUE sensory cortex involvement

Summary

- Physiological brain imaging techniques are rapidly evolving
- These techniques have the potential to improve diagnostic accuracy in patients with brain tumors, AVMs and other conditions
- The additional information afforded by these techniques may help establish prognosis, may be used to monitor therapies, and may influence treatment decisions
- Current applications represent only the initial steps of physiologic brain imaging